retina.[7,11,28] Although not a universal finding in patients with retinal vasculitis, these abnormalities have given support to the hypothesis that retinal vasculitis is an autoimmune disorder. A causal relationship between such abnormalities and retinal vasculitis has never been established, however, and their role in the pathogenesis of the disorder remains speculative. Because these abnormalities have never been shown to have diagnostic, therapeutic, or prognostic significance,[29] they are probably unnecessary in the routine evaluation of retinal vasculitis.

The treatment of patients with retinal vasculitis should be directed toward the underlying systemic problem, if one is identified. Management of the vasculitis per se is necessary only if it is leading to vision-threatening complications. It is important to distinguish between vaso-occlusive inflammatory disease and simple vascular sheathing; fluorescein angiography is a useful tool in making this determination. Aggressive anti-inflammatory therapy is not indicated for patients with asymptomatic vascular sheathing; the use of steroids in such therapy may produce glaucoma and cataracts.

The treatment of occlusive vasculitis has generally been disappointing regardless of the modality used, but corticosteroids have been its mainstay. If there is no systemic disease, the periocular administration of long-acting corticosteroids such as triamcinolone acetonide should be considered to avoid systemic side effects. Topically applied corticosteroids cannot reach the retina.

Immunosuppressive therapy is usually a treatment of last resort, but the literature contains little evidence that it is beneficial for the long-term retention of vision in severe idiopathic retinal vasculitis. The use of immunosuppressive agents for intraocular inflammatory disease is generally reserved for patients with bilateral disease whose vision has fallen below 20/40 in the better eye. Occlusive vasculitis in patients with Behçet's syndrome is the one form of uveitis for which most authorities agree that immunosuppressive drugs are the treatment of first choice. They are best administered by an internist experienced in their use, with monitoring of treatment effect by an ophthalmologist, again indicating the importance of a team approach.

Sometimes complications cannot be avoided despite aggressive therapy. When complications arise, treatment with laser therapy for neovascularization or vitrectomy for hemorrhage is required.

More effective management of retinal vasculitis must await a better understanding of its associated disease mechanisms. Rosenbaum and colleagues have shown that progress is being made toward that understanding. In the meantime, they have provided an excellent framework for developing a rational approach to the current evaluation and management of the disorder.

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Modifying Physician Practice Patterns—Reflections on Past Deeds

THE PRACTICE OF MEDICINE once enjoyed a purity of focus that has only recently begun to change. The traditional physician knew that maximizing the welfare of patients was the order of the day. The health care system, having identified the physician as the patient's agent for that goal, fashioned itself to serve the physician's needs. What worked for the doctor worked for the patient. What worked for the doctor also worked for the hospital, at least for a while.

Now the picture has changed. Patients, physicians, and hospitals, while not having parted ways, have begun to identify their differences. Why has such a change occurred? Most observers agree on the spectrum of reasons, if not the magnitude of their contribution to the change. The explosion of technology with its heightened emphasis on uncertainty; changes in societal attitudes toward risk-taking, conflict resolution, and regulation; growing tensions between the demand for medical care and the supply of that care; and the

presence of new players (that is, payers) have all contributed to the partial dissolution of what once was seen as unity of purpose.[1,2]

With disarray, however, comes opportunity. Some of the same themes that have illuminated the differences among patients, physicians, and hospitals may also serve as the glue that binds them together. A common interest in quality, coupled with a desire for efficiency, has provided an impetus for new approaches to the delivery of health care services.

Among the approaches to achieving optimum cost-effectiveness, modifying physicians' practice patterns has drawn its share of attention. In this issue of the journal, Rosenstein and Stier describe a process—called the Medical Resource Management Program[3]—that relies heavily on the assumption that an important way to improve effectiveness and efficiency is to induce physicians to practice differently. There is little that is new in this assumption because it is known that physicians control the use of the majority of health care resources. What is different is the next assumption: that self-analysis will ultimately improve the efficiency of health care delivery. The emphasis here is on analyzing practice patterns, identifying areas that can be changed, educating about possible changes, and eventually implementing those changes.

Education has generally been viewed as the most desirable approach to modifying physician behavior, but its effectiveness in achieving that goal has been variable.[2,4-6] While a number of studies have shown that education about the prices or cost-effectiveness of various tests and procedures can result in a change in behavior, the economic effects of such changes have generally been modest at best.[7] The result is that other investigators have focused attention on other means of changing behavior: administrative barriers and penalties, incentives, and feedback about current performance.[2,5,8] In each case, there is evidence to suggest that these interventions are capable of inducing some degree of change. Again, however, the results are variable and often unpredictable. It has been argued that this unpredictability stems from several areas. First, the impetus for change often comes from outside the system and thus is resisted by physicians. The increasing development of practice guidelines is an example.[9] These guidelines are usually extremely general and may not fit the needs of the local setting. Second, the tools for change often do not involve practitioners. Physicians are asked to change their behavior but may not be asked how they feel about those changes. Often there are many competing forces that may work for or against achieving a desired goal. The authors of the change may be only vaguely aware of these forces, as opposed to the physician who will be strongly attuned to the presence and magnitude of each of the forces.

Keep in mind that physicians are extraordinarily capable of changing their practice when it seems appropriate to them. Witness the markedly diminished length of stay for acute myocardial infarction[5] and the rapid adoption of new technologies such as computed tomography and magnetic resonance imaging.[10] Most recently, in less time than it took to test whether or not extracorporeal shock wave lithotripsy of gallstones might provide a new way of treating gallbladder disease, physicians have nearly universally embraced laparoscopic cholecystectomy.[11] Given this evidence of rapid practice changes, why do we see strong resistance to other kinds of changes? As indicated earlier, most changes that deal directly with new approaches to cost-effective care involve understanding and manipulating a wide variety of complicated and potentially competing forces. As such, change is likely to occur only when it is driven on a local level where each force can be identified and understood. This is the strength of Rosenstein and Stier's approach.

While the approach proposed in their article is not new, it is still relatively untested. The authors describe the theoretical construct for what appears to be a promising system. Nonetheless, there is still only modest evidence that such an approach is economically justifiable. Earlier work has provided some evidence that change directed by self-analysis can have a substantial effect on selected aspects of practice. The Rosenstein model is an offshoot of an earlier project known as COSTEP, an acronym for "cost-effective practice." The COSTEP project, developed by Sommers and colleagues,[12-14] has now been applied in a number of hospital settings in northern California. In almost every case, the COSTEP project has been able to identify and significantly improve the efficiency of the delivery of care in well-circumscribed areas—length of stay in hip arthroplasty, fewer coronary care unit admissions for patients with chest pain, shorter stays of patients after a prostatectomy, and improved medication ordering for patients having cesarean section.

What do these successful projects have in common? First, they use good information.[15] That is, they have access to data about how care is provided and where potential problems may exist. Second, they depend on formalized reflection on actual practice patterns.[16] This can be viewed as a form of scholarly introspection. Next, they depend on reaching a consensus about how change might occur. There is some evidence to suggest that consensus is most likely to be reached when the instigators of discussion are respected leaders. Sommers and associates argue, moreover, that change is more likely to occur when the complete constituency for change is recognized. In many instances, this implies a closer working relationship between physicians and nurses, not just among physicians. Finally, there is the assumption that once a change occurs, its effect will be monitored through subsequent data analysis. In essence, we are talking about an action-experiment designed to change practice styles. Not only is such an approach theoretically sound, it is likely to be accepted by a wider group of practitioners.

Even then, will such a change make a true economic impact? That remains to be seen. Many physicians are cynical about the ability of any kind of practice change to have real economic effects, given the uncertain relationship between charges and actual costs. Perhaps the primary goal should not necessarily be the diminution of health care costs. In earlier years, physicians rarely concerned themselves with cost issues. While costs are an increasingly important concern to all members of the health care team, quality is still the primary goal. As long as the focus continues to be the efficient provision of high-quality care, it is likely that we will not stray far from the goal of providing cost-effective care. Is there really any other choice?

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Neuro-oncology Is Coming of Age

BIOMEDICAL RESEARCH is founded on the belief that insights into the cellular alterations that are responsible for pathologic disorders will provide a basis on which new approaches to the diagnosis and management of disease might be pursued. Recently, major advances in our understanding of tumor cell biology have dramatically expanded our knowledge of the molecular events that underlie the development of cancer, and these in turn have opened opportunities for the development of new therapeutic approaches not even imaginable a short while ago. The clinical conference in this month's issue of THE WESTERN JOURNAL OF MEDICINE describes new imaging and treatment modalities that hold promise for more effective treatment of patients with brain tumors.[1] Moreover, this report hints at the directions the next generation of studies may lead us. These future studies augur well for the likelihood that even more effective and less toxic approaches to therapy can be developed.

We now know that the panoply of cellular characteristics distinguishing malignant cells from their normal counterparts is orchestrated by the altered expression of genes important for normal cell growth and differentiation. Cancer arises as a disorder of genes. These genes are called oncogenes, emphasizing their importance in the development of tumors, and several have been implicated in the pathogenesis of brain tumors. Among the genes whose normal functions are used pathologically and contribute to the development of central nervous system (CNS) tumors are those that encode molecules important for the transmission of signals regulating cellular processes altered in tumor cells. For example, molecules on the surface of glial cells specifically bind small polypeptides capable of initiating the cascade of molecular events that becomes neoplastic growth. These molecules include the epidermal growth factor receptor and the platelet-derived growth factor receptors.

Membrane signal receptors for growth factors are under close scrutiny by investigators attempting to use them as targets for pharmacologic agents. The specific high-affinity binding of ligands to such receptors provides an efficient mechanism by which to expose tumor cells to molecules that can be imaged diagnostically and to cytotoxic moieties that can be used therapeutically. Cellular toxins, such as ricin, *Pseudomonas* endotoxin, and saprosin, as well as image-enhancing agents, have been conjugated to such ligands. The clinical efficacy of such "magic bullets" is currently being examined.

While such an approach has considerable appeal, investigators must overcome the binding of these hybrid molecules to comparable receptors on normal tissues. As pointed out in the UCLA conference report, it is now widely recognized that the benzodiazepine receptor exists in at least two distinct forms. One, the so-called central receptor, is found primarily in the CNS. A second, functionally distinct receptor, the "peripheral receptor," is prominent in many tissues throughout the body but expressed at only low levels in the CNS. This peripheral benzodiazepine is apparently expressed on glial tumor cells at levels as much as 20-fold higher than those seen on other central nervous system tissues. Interestingly, benzodiazepine ligands may be inhibitors of cell growth under some conditions, and the characterization of this growth regulatory ligand-receptor loop may provide insights into both the etiology and biology of glial tumors. Of immediate clinical import, however, is the possibility that this tumor-specific change might be exploited both diagnostically and therapeutically in studies attempting to target molecules to brain tumors.

If this quantitative difference in receptor expression is the result of enhanced expression of the receptor on all tumor cells, and not simply extremely high levels on a small proportion of malignant cells, it may provide the contrast required to target molecules and thereby distinguish malignant from normal tissue in imaging studies. Also, it may provide sufficient specificity to enhance the therapeutic index of hybrid molecules developed as antineoplastic agents to treat such tumors of the CNS. In this regard, expression of the peripheral benzodiazepine receptor on mitochondrial membranes is of particular interest because it raises the possibility that poisons that inhibit or alter the numerous biochemical processes that are limited to the mitochondria might be pursued as new antineoplastic agents. Of course, the hybrid molecules that would be designed for such targeted approaches to therapy would have to be taken up by CNS tumor cells. Also, the broad distribution of peripheral benzodiazepine receptor expression throughout the body will require the development of strategies to block binding at such sites if therapeutic applications are pursued. Pretreatment of patients with ligand bound to a molecule that could not pass the blood-brain barrier may be one such possibility.

New approaches to the imaging of brain tumors, also discussed at the UCLA conference, may provide additional opportunities to exploit tumor cell-targeted molecular manipulations, such as those mentioned. While surgical treatment and external beam irradiation remain our most effective modalities for the management of patients with brain tumors, their application could be greatly enhanced by a better understanding of the tumor-normal tissue interface. This information would allow more effective treatment with less toxicity. Positron emission tomography makes it possible noninva-